I. AMENDMENTS

In the claims:

43. (Amended) The gene delivery vector according to claim 34 where said vector is a eukaryotic layered vector initiation system vector.

Attached hereto is a **version showing changes made to the claims** and a **currently pending claim set.**

II. REMARKS

Claims 26, 28-31 and 33-44 are pending and stand rejected under 35 U.S.C. §§ 112, second paragraph and 103. Claim 43 has been amended herein to clarify that the vector is a eukaryotic layered vector initiation system vector, as described throughout the specification. No new matter has been added a result of this amendment and entry thereof is respectfully requested. As can be seen by the nature of the amendment, it is also noted that this amendment is made for reasons unrelated to patentability.

In view of the foregoing amendment and following remarks, Applicants request reconsideration of the application and claims.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected all pending claims as allegedly indefinite. In support of this rejection, the Examiner states:

> One aspect of claim 26 is drawn to encoding a viral agent from a pathogenic agent. Claim 28 states that the antigen is a viral antigen and claim 30 states that the pathogenic agent is a bacteria, parasite or fungus. Does this mean that the viral antigen is derived only from viruses that infect bacteria, parasites, or fungus? However, this is clearly not what

> applicant intends because claim 29 lists various viruses that infect humans and felines, and not any of the other pathogenic agents listed in claim 30. This rejection is merely to bring this inconsistency to applicant's attention. (Office Action, page 2).

Applicants traverse the rejection. Independent claim 26 is drawn to an expression cassette comprising two promoters. The second promoter is operably linked to a nucleic acid molecule encoding an antigen from a pathogenic agent. To those working in this area (and as used in the specification), the terms "agent" and "antigen" are quite different. In this regard, Applicants direct the Examiner's attention to the fact that claim 26 does not require the antigen to be a viral antigen. Indeed, it is only in dependent claims 28 and 29 that the antigen is specified as being a viral antigen. For its part, claim 30 depends only from claim 26 -- thus, the antigen in this claim is obtained from the specified pathogenic agent (i.e. bacteria, fungus or parasite). Therefore, Applicants believe the claims are clear and that they contain the proper dependencies. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. 103(a)

All of the pending claims stand rejected as allegedly obvious over U.S. Patent No. 6,015,686 (hereinafter "Dubensky"); Polo et al. (hereinafter "Polo") and Cella et al. (hereinafter "Cella"). Specifically, it is alleged that the eukaryotic vector initiation system cassettes taught by Dubensky include all the elements of the pending claims except the expression of dsRNA. (See, Office Action, page 4). It is further alleged that one of skill in the art would have been motivated to express dsRNA in view of the teachings of Cella and Polo. (Office Action, pages 4-5).

Because the references do not teach or suggest the invention as claimed, Applicants traverse the rejection.

The Examiner bears the burden of establishing a *prima facie* case of obviousness. *See, e.g., In re Ryckaert,* 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); and *In re Oetiker,* 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). It is well settled that even when references relied upon teach that all aspects of the claimed invention are known individually in the art, *prima facie* obviousness is not established without some objective reasoning to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (BPAI 1993). Thus, even if individual elements of the invention are taught in the prior art, such is not, in and of itself, sufficient to make out a case of *prima facie* obviousness. See, *Symbol Technologies, Inc. v. Opticon, Inc.*, 19 USPQ2d 1241 (Fed. Cir. 1991) ("We do not pick and chose among the individual elements of assorted prior art references to recreate the claimed invention, but rather, we look for some teaching or suggestion in the references to support their use in the particular claimed combination."). As stated by the Court of Appeals for the Federal Circuit, "[i]t is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *In re Fritch*, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992). See, also, *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988): "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." and *In re Laskowski,* 10 USPQ2d 1397, 1399 (Fed. Cir. 1989) stating that "the mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification."

Applicants submit that the Examiner has failed to make out a *prima facie* case of obviousness because the combination of references does not teach or suggest each and every element of the claimed invention recited. Further, there is simply no motivation within the cited references to arrive at the claimed invention and no reasonable expectation of success.

The claimed invention is drawn to an expression cassette comprising two promoters. One promoter is operably linked to a nucleic acid molecule which, when transcribed *in vivo* forms a double stranded RNA that induces the production of interferon. In addition, the expression cassette also comprises an RNA Polymerase II promoter operably linked to a nucleic acid molecule encoding an antigen obtained from a pathogenic agent.

The primary reference, Dubensky, describes and claims eukaryotic layered vector initiation systems (ELVIS) and expression constructs used in these systems. As acknowledged by the Office, this reference is silent as to the formation of a double stranded RNA that induces production interferon. (See, Office Action page 3). Moreover, unlike the pending claims, Dubensky's constructs do not contain an RNA polymerase II promoter operably linked to a nucleic acid molecule encoding an antigen obtained from a pathogenic agent. Further, the RNA Pol II promoter used by Applicants is a DNA-dependent RNA promoter. In contrast, Dubensky's ELVIS constructs use an RNA-dependent RNA promoter operably linked to a nucleic acid encoding a heterologous sequence. Thus, Dubensky fails to teach or suggest key elements of the pending claims.

Both Polo and Cella fail to supply what is missing from Dubensky. Indeed, these references are completely silent as to expression constructs having two promoters, wherein the promoter operably linked to the nucleic acid molecule encoding an antigen is an RNA polymerase II promoter.

For the foregoing reasons and the reasons of record, Applicants submit that the references, alone or in combination, do not render the invention as claimed obvious.

III. CONCLUSION

In view of the foregoing, Applicants submit that the claims are now in condition for allowance and requests early notification to that effect.

Please direct all further communications regarding this application to:

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Version Showing Changes Made to Claims

43. (Amended) The gene delivery vector according to claim 34 where said vector is a eukaryotic layered vector initiation system vector.

Currently Pending Claims

26. An expression cassette comprising a promoter operably linked to a nucleic acid molecule which, when transcribed *in vivo*, forms double stranded RNA that induces the production of interferon, and an RNA polymerase II promoter operably linked to a nucleic acid molecule that encodes an antigen from a pathogenic agent.

28. The expression cassette according to claim 26 wherein said antigen is a viral antigen.

29. The expression cassette according to claim 28 wherein said viral antigen is selected from the group consisting of HIV, HSV, HBV, HCV, HPV, and FIV.

30. The expression cassette according to claim 26 wherein said pathogenic agent is a bacteria, parasite or fungus.

31. The expression cassette according to claim 26 wherein said pathogenic agent is a tumor.

33. The expression cassette according to claim 26 wherein said pol II promoter is selected from the group consisting of CMV, SV40, MoMLV LTR and RSV LTR.

34. A gene delivery vector, comprising an expression cassette according to claim 26.

35. The gene delivery vector according to claim 34 where said vector is a plasmid.

36. The gene delivery vector according to claim 34 where said vector is a recombinant retrovirus.

37. The gene delivery vector according to claim 34 where said vector is a recombinant herpesvirus.

38. The gene delivery vector according to claim 34 where said vector is a recombinant poxvirus.

39. The gene delivery vector according to claim 34 where said vector is a recombinant adenovirus.

40. The gene delivery vector according to claim 34 where said vector is a recombinant parvovirus.

41. The gene delivery vector according to claim 34 where said vector is a recombinant alphavirus.

42. The gene delivery vector according to claim 34 where said vector is a recombinant polyoma virus.

43. (Amended) The gene delivery vector according to claim 34 where said vector is a eukaryotic layered vector initiation system vector.

44. A cell which contains a gene delivery vector according to claim 34.